DETAILED ACTION

Status of the Claims

Claims 1-31 are pending.

Amendment to claims 1, 2, 5-11, 14, 19, 23-25, 27-30 and 31 are acknowledged.

Currently, claims 23-31 are pending and under examination.

Withdrawn Rejections

All previous rejections of the claims under 35 U.S.C. 103, not reiterated herein, are withdrawn in view of Applicant's amendments and arguments filed 10 June 2008.

Election/Restrictions

Applicant's election of Group II, claims 23-31 in the reply filed on 21 July 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The restriction is made FINAL.

Claim Objections

Claim 23 is objected to because of the following informalities: the phrase "substantially accurately," is considered superfluous and the examiner recommends removal from the claim.

35 USC § 112, sixth paragraph

The following is a quotation of the sixth paragraph of 35 U.S.C. 112:

> An element in a claim for a combination may be expressed as a means or step for performing a specified function without the recital of structure, material, or acts in support thereof, and such claim shall be construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof.

Applicant's recitation of "means for substantially accurately dispensing the pharmaceutical solution…" and "…the means for dispensing…" in claims 23 and 25, respectively, has invoked the special claim interpretation provisions of 35 USC 112 sixth paragraph.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's recitation of "means for substantially accurately dispensing the pharmaceutical solution…" and "…the means for dispensing…" in claims 23 and 25, respectively, has invoked the special claim interpretation provisions of 35 USC 112, sixth paragraph, as set forth above. In turn, claim 23 and all dependent claims thereof (i.e. claims 24-31) are rejected under 35 USC 112, second paragraph.

In order for a claim to meet the particularity requirement of 35 USC 112 second paragraph, the corresponding structure(s) of a means-plus-function limitation must be

disclosed in the written description in such a manner that one skilled in the art will know and understand what structure corresponds to the means limitation.

Regarding the means-plus-function limitations recited in the instant claim, i.e., "means for substantially accurately dispensing the pharmaceutical solution…" and "…the means for dispensing…" there is ambiguity as to which structural components, disclosed in the specification, the applicant regards as the, "means for substantially accurately dispensing the pharmaceutical solution...". For example, it is unclear if the "means for dispensing" comprises the fluid dispenser 16 including an array 24 of fluid drop generators and reservoirs 18, 20, and 22 of Figure 1; the fluid dispenser and all its corresponding elements in Figure 2; the fluid ejection cartridge of Figure 3; or the firing chamber of Figure 4.

Therefore, if there is no structure in the specification that clearly corresponds to the means-plus-function limitation in the claims, the claim will be found invalid as being indefinite.

The terms "substantially highly concentrated" and "substantially low volume" in claim 24 are relative terms which render the claim indefinite. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The concepts to which Applicant refers might more aptly be described as "highly concentrated" and "very low volume" or "picoliter volume," respectively. The instant Specification tends to support such a characterization.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 23-25 and 27-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over **TOKIE** (US Patent 6,513,897, issued 4 February 2003).

Independent claim 23 is drawn to:

A pharmaceutical dispensing apparatus including a fluid dispenser having a piezoelectric fluid ejection device or a thermal fluid ejection device for dispensing a pharmaceutical solution including an active pharmaceutical ingredient dissolved in a vehicle, comprising:
means for substantially accurately dispensing the pharmaceutical solution at a predetermined dosage within a variation of reproducibility of less than about 15%;
wherein the vehicle is configured to, or exposed to conditions sufficient to substantially prevent instability of the active pharmaceutical ingredient during the dispensing of the pharmaceutical solution.

TOKIE teaches a piezoelectric or thermal fluid dispensing system for dispensing fluid material onto a substrate, wherein the fluid materials may include solvent-based solutions (as seen as applicant's instant vehicle) containing one or more additive

components, which may include pharmaceutical compounds (Abstract; column 5, line 66 to column 6 line 2; column 6, lines 39-43; column 9, lines 17-20 and 44-48).

With respect to the specifically recited variation of reproducibility in claim 1 and 27, TOKIE teaches accurate, reliable, and repeatable deposition of fluid materials (column 8, line 66 to column 8, line 2; column 11, line 48-42), but does not specifically teach a variation of reproducibility of less than 15%. Additionally, TOKIE does not teach the ranges of variation of reproducibility recited in claims 28-30.

However, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value for a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation," Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art."

Applicant has not disclosed that the specific limitations recited in instant claims 1 and 27-30 are for any particular purpose or solve any stated problem, and the prior art teaches that fluid deposition may be varied because different deposition patterns or sizes may be desired. Absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the prior art by normal optimization procedures know in the liquid dispensing art.

With respect to applicant's recitation of a,"…vehicle configured to, or exposed to conditions sufficient to substantially prevent instability of the active pharmaceutical ingredient (API)," in claim 23, TOKIE teaches pharmaceutical compounds as additives to fluid materials, which include solvent-based solutions, but does not explicitly discuss the solvent-based solution preventing instability of the API. However, the applicant has stated that the vehicle into which the API is dissolved includes at least one solvent (page 9, line 15-16). Therefore, since TOKIE teaches pharmaceutical compounds in solvent-based solutions it is asserted that TOKIE meets the limitation of preventing instability of the API during dispensing.

With respect to the phrase, "means for dispensing," in claims 23 and 25, TOKIE teaches the jettable material (as seen as applicant's instant API dissolved in the vehicle) is supplied to the piezoelectric ink jet from a reservoir (as seen as applicant's instant means for dispensing) (Figure 2, items 120, 127, and 128; column 6, lines 10-31). Due to the ambiguity related to the means for dispensing, the "means for dispensing" is interpreted, in rejection of claims 23 and 25, as comprising a fluid dispenser and reservoir.

With respect to claim 24, TOKIE teaches that the fluid dispensing system described above is able to achieve an approximate drop volume of 100 picoliters (as seen as applicant's instant low volume) (column 6, line 46). Furthermore, TOKIE teaches pharmaceutical compounds as additives to fluid materials, which would indicate that the pharmaceutical compound is present at some concentration within the low volume droplets. TOKIE does not explicitly teach that the API is highly concentrated.

However, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (MPEP 2144.05).

With respect to claim 27, TOKIE teaches that the substrate onto which the droplets are dispensed may include one or more types of materials (e.g. papers, polymeric films, laminates, metals, etc.) (column 4, lines 41-52). As mentioned above, the variation of reproducibility is not granted significant patentable weight as it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value for a result effective variable.

With respect to claim 31, TOKIE teaches a pharmaceutical compound as an additive to a solvent-based solution, but does not discuss the solubility of said compounds.

However, the solubility of a pharmaceutical compound is an inherent physical property that is directly related to the concentration of a pharmaceutical compound solution that can be prepared. The adjustment of particular conventional working conditions (e.g., determining result effective amounts of the ingredients beneficially taught by the cited references) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the artisan of ordinary skill. Accordingly, manipulation of the amounts of solute and solvent in the preparation of

solutions for dispensing or testing would have been well within the purview of the person of ordinary skill in the art and no more than an effort to optimize results.

4. Claims 23-25 and 27-30 rejected under 35 U.S.C. 103(a) as being unpatentable over **Bernardini et al.** (*Journal of Neuroscience Methods*, 1991, Vol. 38, pages 81-88) (hereinafter as "BERNARDINI").

BERNARDINI teaches piezoelectric driven fluid ejection devices for dispensing active pharmaceutical ingredients (e.g. as shown in reference as dopamine) dissolved at predetermined dosages in vehicle (e.g. as shown in reference as deionized water) onto various substrates (Abstract).

With respect to the specifically recited variation of reproducibility in claim 1 and 27, BERNARDINI teaches dispensing precise volumes (i.e. dosages) of fluid (i.e. pharmaceutical ingredients) using the disclosed device, but does not specifically teach a variation of reproducibility of less than 15% (page 83, right column, 2nd full paragraph, lines 12-13; page 85, right column, 1st full paragraph, line 4; page 87, left column, 1st paragraph, line 1). Additionally, BERNARDINI does not teach the ranges of variation of reproducibility recited in claims 28-30.

However, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value for a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation," Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No

invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art."

Applicant has not disclosed that the specific limitations recited in instant claims 1 and 27-30 are for any particular purpose or solve any stated problem, and the prior art teaches that fluid deposition may be varied because different deposition patterns or sizes may be desired. Absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the prior art by normal optimization procedures know in the liquid dispensing art.

With respect to applicant's recitation of a,"…vehicle configured to, or exposed to conditions sufficient to substantially prevent instability of the active pharmaceutical ingredient (API)," in claim 23, BERNARDINI teaches dopamine dissolved in deionized (DI) water, but does not explicitly discuss the solvent-based solution preventing instability of the API (page 83, right column, 1st full paragraph, lines 10-14). However, the applicant has stated that the vehicle into which the API is dissolved includes at least one solvent (page 9, line 15-16). Therefore, since BERNARDINI teaches dopamine in DI water, wherein the neuroactive compound was able to stimulate neuronal responses, it is asserted that BERNARDINI meets the limitation of preventing instability of the API during dispensing (page 85, right column, 1st full paragraph, lines 1-6).

With respect to the phrase, "means for dispensing," in claims 23 and 25, BERNARDINI teaches piezoelectric dispensing jets made by fusing a piezoelectric

crystal to the side of a capillary pipette, which is connected to a reservoir from which the dispensed fluid material is obtained (page 82, left column, 1st full paragraph, lines 1-5; right column, 1st full paragraph, lines 1-10). Due to the ambiguity related to the means for dispensing, the "means for dispensing" is interpreted, in rejection of claims 23 and 25, as comprising a fluid dispenser and reservoir.

With respect to claim 24, BERNARDINI teaches that the fluid dispensing system described above is able to achieve an approximate drop volume of 70 picoliters (as seen as applicant's instant low volume) (Abstract). Furthermore, BERNARDINI teaches 2-10 mM of dopamine dissolved in DI water. BERNARDINI does not explicitly teach that the API is highly concentrated.

However, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (MPEP 2144.05).

With respect to claim 27, BERNARDINI teaches the piezoelectric dispensing device is used to dispense fluid materials onto at least two mediums (e.g. as shown in reference as frozen tissue sections and brain tissue slices) (Abstract). As mentioned above, the variation of reproducibility is not granted significant patentable weight as it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value for a result effective variable.

With respect to claim 31, BERNARDINI teaches the piezoelectric driven fluid ejection apparatus for dispensing various concentrations of dopamine dissolved in DI water to various mediums, as discussed above, but does not discuss the solubility of said compounds.

However, the solubility of a pharmaceutical compound is an inherent physical property that is directly related to the concentration of a pharmaceutical compound solution that can be prepared. The adjustment of particular conventional working conditions (e.g., determining result effective amounts of the ingredients beneficially taught by the cited references) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the artisan of ordinary skill. Accordingly, manipulation of the amounts of solute and solvent in the preparation of solutions for dispensing or testing would have been well within the purview of the person of ordinary skill in the art and no more than an effort to optimize results.

5. Claims 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over **BERNARDINI** (*J. of Neuroscience Methods*, 1991, Vol. 38, pages 81-88) as applied to claim 25 above, and further in view of **Cook et al.** (The American Journal of Surgery, 1983, Vol. 146, Issue 6, pages 807-810) (hereinafter as "COOK").

BERNARDINI teach the piezoelectric driven fluid ejection appartus for dispensing dopamine to various mediums, as discussed above. However, BERNARDINI fails to teach that the ingredient is digoxin.

COOK teaches the combinational of therapy of digoxin and dopamine in treating postoperative patients with cardiac dysfunction. The results of COOK indicate that the inotropic effects of dopamine and digoxin are additive when given in combination and that digoxin can be used to significantly reduce the dopamine dosage in patients with postoperative cardiac failure (page 809, Summary).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute digoxin, taught by COOK, with dopamine as the pharmaceutical ingredient used in the piezoelectric fluid ejection device taught by BERNARDINI.

One having ordinary skill in the art would have been motivated to make such a change as a mere alternative and functionally equivalent pharmaceutical ingredient and since the same expected fluid dispensing results would have been obtained. The use of alternative and functionally equivalent ingredients would have been desirable to those of ordinary skill in the art based on the desired drug treatment regimen and/or the desired drug mechanism of action.

Response to Arguments

6. Applicant's arguments with respect to claims 23-31 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Erik B. Crawford whose telephone number is (571)270-1011. The examiner can normally be reached on Monday through Friday, 8:00am to 5:00pm.

Prior to May 20th, if attempts to reach the examiner by telephone are unsuccessful, the examiner's Acting Supervisor, Mr. James O. Wilson can be reached on (570)272-0661. After May 20th, if attempts to reach the examiner by telephone are unsuccessful, please contact Mark Shibuya, SPE 1641 at (571)272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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